**Supplementary Materials: Respiratory Syncytial Virus Infection among Hospitalized Infants in Four Middle-Income Countries**

**Table of Contents**

**Supplementary Table 1:** Characteristics of Study Countries and Hospital Enrollment Sites

**Supplementary Table 2:** Demographic and Clinical Characteristics of All Enrolled Hospitalized Infants in Albania, Jordan, Nicaragua and the Philippines

**Supplementary Table 3:** Clinical Course and Treatment during Hospitalization of Infants with Respiratory Syncytial Virus (RSV) Infection by Age Group

**Supplementary Table 4:** Maternal Health and Sociodemographic Factors and Illness Severity among Hospitalized RSV-Positive Infants, All Sites

**Supplementary Figure 1:** Screening and Enrollment of Hospitalized Infants

**Supplementary Figure 2:** (A) Number and Percentage of Infants Positive for Respiratory Syncytial Virus (RSV) by Age in Months, All Sites (B) Percentage of RSV-Positive Infants with Detectable Anti-RSV Antibodies in Acute-Phase Serum by Age in Months.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **City, Country** | **World Bank income classification\*** | **Climate** | **Study Hospital** | | | **Local population served** | **Enrollment period** |
| **Site** | **No. general pediatric beds** | **No. pediatric ICU beds** |
| Tirana, Albania | Upper-middle | Temperate | Pediatric Department University Hospital “Mother Theresa” | 88 | 25 | ~610,000 | Year 1: 12/1/2015–5/2/2016  Year 2: 11/2/2016–4/15/2017 |
| Maternity Hospital “Queen Geraldine” Neonatology Unit | 19 | 5 |
| Amman, Jordan | Lower-middle (2016); Upper-middle (2015, 2017) | Temperate | Al-Basheer Hospital, Maternal and Pediatric Building | 120 | 70 | ~4 million | Year 1: 12/27/2015–5/2/2016 Year 2: 11/13/2016—4/20/2017 |
| Managua, Nicaragua | Lower-middle | Tropical | Hospital Infantil Manual De Jesus Rivera “La Mascota” | 270 | 31 | ~1 million | Year 1: 6/26/2015–1/29/2016  Year 2: 5/23/2016—3/3/2017 |
| Bohol Island, Philippines | Lower-middle | Tropical | Governor Celestino Gallares Memorial Regional Hospital | 42 | 8 | ~1.4 million | 10/1/2015 – 12/28/2016 |

**Supplementary Table 1. Characteristics of Study Countries and Hospital Enrollment Sites**

\* The World Bank Country and Lending Groups. (Accessed November 14, 2018, at <https://datahelpdesk.worldbank.org/knowledgebase/articles/906519>.)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **All sites**  **N=3634**  **No. (%)** | **Albania**  **N=1032**  **No. (%)** | **Jordan**  **N=1057**  **No. (%)** | **Nicaragua**  **N=937**  **No. (%)** | **Philippines**  **N=608**  **No. (%)** |
| Age, mo. |  |  |  |  |  |
| Median (IQR) | 3.1 (1.0-7.0) | 4.2 (1.7-7.5) | 1.6 (0.4-3.5) | 4.1 (1.2 -7.9) | 5.2 (1.5-8.1) |
| Age group, mo. |  |  |  |  |  |
| <1 | 889 (24) | 157 (15) | 407 (39) | 202 (22) | 123 (20) |
| 1 | 525 (14) | 142 (14) | 200 (19) | 121 (13) | 62 (10) |
| 2 | 369 (10) | 119 (12) | 143 (14) | 71 (8) | 36 (6) |
| 3 | 244 (7) | 85 (8) | 67 (6) | 67 (7) | 25 (4) |
| 4 | 255 (7) | 88 (9) | 45 (4) | 67 (7) | 55 (9) |
| 5 | 216 (6) | 77 (7) | 39 (4) | 60 (6) | 40 (7) |
| 6 to 8 | 598 (16) | 197 (19) | 90 (9) | 163 (17) | 148 (24) |
| 9 to 11 | 538 (15) | 167 (16) | 66 (6) | 186 (20) | 119 (20) |
| Sex |  |  |  |  |  |
| Male | 2099 (58) | 586 (57) | 603 (57) | 534 (57) | 376 (62) |
| Female | 1535 (42) | 446 (43) | 454 (43) | 403 (43) | 232 (38) |
| Infant medical and birth history (parent report) |  |  |  |  |  |
| Preterm birtha | 336/3492 (9) | 73/993(7) | 132/1045 (13) | 78/863 (9) | 44/591 (7) |
| Very preterm birthb | 46/3492 (1) | 10/993 (1) | 14/1045 (1) | 11/863 (1) | 11/591 (2) |
| Low birth weightc | 555/3428 (16) | 89/1000 (9) | 247/1029 (24) | 87/836 (10) | 132/563 (23) |
| Vaginal delivery | 2362/3559 (66) | 646/1011 (64) | 668/1045 (64) | 513/909 (56) | 535/594 (90) |
| Delivery by caesarean section | 1197/3559 (34) | 365/1011 (36) | 377/1045 (36) | 396/909 (43) | 59/594 (10) |
| Underlying medical conditiond | 238 (7) | 72 (7) | 87 (8) | 47 (5) | 32 (5) |
| Low weight-for-age z-scoree | 661/3504 (19) | 93/991 (9) | 271/1006 (27) | 118/910 (13) | 179/597 (30) |
| Sociodemographic factors |  |  |  |  |  |
| Maternal age, yr. |  |  |  |  |  |
| ≤ 19 | 482 (13) | 53 (5) | 104 (10) | 264 (28) | 61 (10) |
| 20 to 24 | 1083 (30) | 257 (25) | 326 (31) | 318 (34) | 182 (30) |
| 25 to 29 | 999 (27) | 379 (37) | 275 (26) | 199 (21) | 146 (24) |
| 30 to 34 | 655 (18) | 233 (23) | 213 (20) | 111 (12) | 98 (16) |
| 35 to 39 | 321 (9) | 92 (9) | 121 (11) | 35 (4) | 73 (12) |
| ≥ 40 | 94 (3) | 18 (2) | 18 (2) | 10 (1) | 48 (8) |
| Attends daycare | 65 (2) | 44 (4) | 14 (1) | 7 (1) | 0 |
| Other children <5-years-old in  home | 1694 (47) | 359 (35) | 653 (62) | 348 (37) | 334 (55) |
| Household crowdingf | 1001 (28) | 151 (15) | 143 (14) | 451 (48) | 256 (42) |
| ≥1 indictor of deprivationg | 904 (25) | 39 (4) | 74 (7) | 221 (24) | 570 (94) |
| Smoking in homeh | 1879 (52) | 391 (38) | 775 (73) | 356 (38) | 357 (59) |
| Currently breastfeeding | 2789 (77) | 855 (83) | 726 (69) | 740 (79) | 468 (77) |
| Sought care for current illness before hospitalization | 1331 (37) | 401 (39) | 408 (39) | 317 (34) | 205 (34) |
| Symptoms (parent report) |  |  |  |  |  |
| Fever or felt hot | 1965 (54) | 623 (60) | 377 (36) | 566 (61) | 399 (66) |
| Chills | 344 (9) | 76 (7) | 180 (17) | 69 (7) | 19 (3) |
| Cough | 2287 (63) | 693 (67) | 629 (60) | 590 (63) | 375 (62) |
| Difficulty breathing | 1830 (50) | 543 (53) | 602 (57) | 464 (50) | 221 (36) |
| Wheezing | 1209 (33) | 142 (14) | 525 (50) | 332 (35) | 210 (35) |
| Rhinorrhea | 1709 (47) | 526 (51) | 324 (31) | 571 (61) | 288 (47) |
| Lethargy | 627 (17) | 107 (10) | 342 (32) | 150 (16) | 28 (5) |
| Excessive crying | 996 (27) | 181 (18) | 314 (30) | 431 (46) | 70 (12) |
| Poor feeding | 1399 (39) | 385 (37) | 551 (52) | 347 (37) | 116 (19) |
| Vomiting | 1100 (30) | 269 (26) | 340 (32) | 320 (34) | 171 (28) |
| Diarrhea | 920 (25) | 169 (16) | 257 (24) | 379 (40) | 115 (19) |

**Table 1. Demographic and Clinical Characteristics of All Enrolled Hospitalized Infants in Albania, Jordan, Nicaragua and the Philippines**

a. Parent-reported gestational age <37 weeks (reported gestational age available for 3,492)

b. Parent-reported gestational age <32 weeks (reported gestational age available for 3,492)

c. Parent-reported birth weight <2.5 kg (reported birth weight available for 3,428)

d. Parent report of any ongoing medical problem diagnosed by a healthcare provider that started at birth or lasted at least 2 weeks

e. Weight-for-age z-score <-2; denominators reflect missing data for weight for some infants or exclusions for outlier values (z-score less than −5 or >5).

f. ≥5 persons in household, including infant

g. Indicators of deprivation include: lack of electricity, presence of an earth floor, or lack of an indoor private flush toilet (or water-sealed toilet for the Philippines)

h. Daily, weekly or monthly smoking in home

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **All Ages**  **N=1129**  **No. (%)** | **0 - 2 mo.**  **N= 600**  **No. (%)** | **3 - 5 mo.**  **N= 241**  **No. (%)** | **6 - 8 mo.**  **N= 167**  **No. (%)** | **9 -11 mo.**  **N= 121**  **No. (%)** |
| Duration of illness before admission – median (range) days | 3 (0-10) | 3 (0-10) | 3 (0-9) | 3 (0-10) | 3 (0-8) |
| Caesarian delivery | 378/1103 (34) | 208 (34) | 80 (34) | 58 (36) | 32 (27) |
| Low birth weight | 154 (14) | 90 (16) | 36 (16) | 18 (12) | 10 (9) |
| Preterm birth | 89 (8) | 48/585 (8) | 25/204 (11) | 10/157 (6) | 6/114 (5) |
| Low weight-for-age-z-score | 170/1093 (16) | 102/581 (18) | 40/231 (17) | 14/165 (8) | 14/116 (12) |
| Very severe illness | 583 (52) | 392 (65) | 107 (44) | 49 (29) | 35 (29) |
| Highest level of care |  |  |  |  |  |
| ICU a | 358 (32) | 252 (42) | 59 (24) | 27 (16) | 20 (17) |
| General ward | 771 (68) | 348 (58) | 182 (76) | 140 (84) | 101 (83) |
| Vital signs b |  |  |  |  |  |
| Fever (≥38⁰C) | 475 (42) | 211 (35) | 102 (42) | 94 (56) | 68 (56) |
| Tachypnea c | 329/976 (34) | 136/491 (28) | 93/220 (42) | 66/159 (42) | 34/106 (32) |
| Hypoxemia (SpO2 <92%) | 448/837 (54) | 322/486 (66) | 69/170 (41) | 38/111 (34) | 19/70 (27) |
| Clinical interventions and treatment |  |  |  |  |  |
| Supplemental oxygen (O2) | 505 (45) | 340 (57) | 97 (40) | 41 (25) | 27 (22) |
| Highest level of O2 support |  |  |  |  |  |
| Non-invasive ventilation d | 10 (1) | 7 (1) | 1 (<1) | 2 (1) | 0 |
| Mechanical ventilation | 20 (2) | 14 (2) | 5 (2) | 1 (1) | 0 |
| IV Fluids | 650 (58) | 355 (59) | 128 (53) | 97 (58) | 70 (58) |
| Tube feeding | 77 (7) | 62 (10) | 9 (4) | 6 (4) | 0 |
| Inotropes | 40 (4) | 28 (5) | 10 (4) | 1 (1) | 0 |
| Antibiotics | 1083 (96) | 573 (96) | 232 (96) | 163 (98) | 115 (95) |
| Corticosteroids |  |  |  |  |  |
| Inhaled | 29 (3) | 20 (3) | 3 (1) | 5 (3) | 1 (<1) |
| Systemic | 390 (35) | 169 (28) | 109 (45) | 70 (42) | 42 (35) |
| Both | 47 (4) | 23 (4) | 10 (4) | 7 (4) | 7 (6) |
| CXR interpretation of pneumonia e | 522/1088 (52) | 265/528 (50) | 111/225 (49) | 86/148 (58) | 60/106 (57) |
| Length of stay – median (range) days | 6 (0-37) | 6 (0-37) | 5 (0-37) | 5 (0-35) | 5 (0-26) |
| Primary discharge diagnosis |  |  |  |  |  |
| Bronchiolitis | 362 (32) | 184 (31) | 101 (42) | 51 (31) | 26 (21) |
| Pneumonia f | 532 (47) | 275 (46) | 112 (46) | 80 (48) | 65 (54) |
| Pertussis-like syndrome | 46 (4) | 39 (7) | 6 (2) | 0 | 1 (1) |
| Sepsis | 45 (4) | 42 (7) | 2 (1) | 0 | 1 (1) |
| Other respiratory diagnosis g | 44 (4) | 20 (3) | 5 (2) | 10 (6) | 9 (7) |
| Other non-respiratory diagnosis g | 91 (8) | 35 (6) | 14 (6) | 24 (14) | 18 (15) |
| Not documented | 9 (1) | 5 (1) | 1 (<1) | 2 (1) | 1 (1) |
| Outcome |  |  |  |  |  |
| Died | 9 (1) | 4 (1) | 3 (1) | 2 (1) | 0 |
| During hospitalization | 4 (<1) | 3 (1) | 1 (<1) | 0 | 0 |
| After hospital transfer | 1 (<1) | 1 (<1) | 0 | 0 | 0 |
| After discharge (within 30 days) | 4 (<1) | 1 (<1) | 1 (<1) | 0 | 2 (2) |
| Readmitted within 30 days | 21 (2) | 9 (2) | 6 (2) | 1 (1) | 5 (4) |

**Supplementary Table 3. Clinical Course and Treatment during Hospitalization of Infants with Respiratory Syncytial Virus (RSV) Infection by Age Group**

a. Includes 9 for which a determination was made that the infant needed ICU care but was not available

b. Any instance recorded during hospitalization

c. Defined as ≥60 breaths per minute for infants <2 months old and ≥50 breaths per minute for infants 2-12 months old

d. Includes CPAP or BiPAP

e. Radiologist or physician interpretation of pneumonia

f. Includes unspecified pneumonia, bacterial pneumonia, viral pneumonia, bronchial pneumonia and consolidated pneumonia

g. Respiratory diagnoses include reactive airway disease, viral respiratory illness, upper respiratory illness, otitis media, bronchitis, transient tachypnea of the newborn; non-respiratory diagnoses include bacteremia, dehydration, seizure, meningitis, urinary tract infection, non-respiratory viral illness, diarrhea/gastroenteritis.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Severe illness**  **N=546**  **No. (%)** | **Very severe illness**  **N=583**  **No. (%)** | **Crude odds ratio**  **(95% CI)** | **Adjusted odds ratioa**  **(95% CI)** |
| Maternal chronic illness | 26 (5) | 25 (4) | 0.9 (0.5-1.6) | 0.7 (0.4-1.3) |
| Pregnancy complication | 115 (22) | 105 (18) | 0.8 (0.6-1.1) | 0.8 (0.6-1.1) |
| Household crowdingb | 165 (30) | 106 (19) | 0.5 (0.4-0.7) | 0.8 (0.6-1.1) |
| Other children <5 years old in home | 272 (50) | 311 (53) | 1.2 (0.9-1.5) | 0.9 (0.7-1.2) |
| Attends daycare | 7 (1) | 13 (2) | 1.8 (0.7-5.2) | 1.7 (0.6-4.7) |
| Smoking in household |  |  |  |  |
| Less than monthly or never | 282 (52) | 270 (46) | ref | ref |
| Daily, weekly or monthly | 262 (48) | 312 (54) | 1.2 (1.0-1.6) | 1.0 (0.8-1.3) |

**Supplementary Table 4. Maternal Health and Sociodemographic Factors and Illness Severity among Hospitalized RSV-Positive Infants, All Sites**

a. Individual variables adjusted for categorical age, sex, site, and preterm birth.

b. ≥5 persons in household, including infant

**3897 infants eligible to enroll**

**3634 enrolled and completed study**

201 Did not consent

35 Missing critical study information

27 Missing laboratory data

**4031 infants approached for screening**

**5959 infants passed prescreening checklist**

**8127 infants prescreened**

**9523 infant admissions reviewed**

1388 Reviewed >24 hours after admission

8 Did not meet age requirement

1911 Outside catchment area

65 Illness duration >10 days

192 Chief admission complaint not acute illness

1912 Not approached for screening

112 Declined participation in screening

22 Illness onset unknown or >10 days since onset

**Supplementary Figure 1. Screening and Enrollment of Hospitalized Infants**

**Supplementary Figure 2.** **A. Number and Percentage of Hospitalized Infants Positive for Respiratory Syncytial Virus (RSV) by Age in Months, All Sites (total number RSV-positive=1129). B. Percentage of RSV-Positive Infants with Detectable Anti-RSV Antibodies in Acute-Phase Serum by Age in Months (total tested n=875).**